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GHB Bibliography and Summary of Medical Articles
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Prolonged Withdrawal From Extreme gamma-Hydroxybutyrate (GHB) Abuse., Mahr G, Bishop CL, Orringer DJ., Psychosomatics 2001 Oct;42(5):439-440. No Abstract available on line PUBMED.

Pentobarbital for severe gamma-butyrolactone withdrawal., Sivilotti ML, Burns MJ, Aaron CK, Greenberg MJ., Ann Emerg Med 2001 Dec;38(6):660-5.

Study Objective: Gamma-hydroxybutyrate (GHB) and gamma-butyrolactone (GBL) have become popular drugs of abuse. Acute overdose with either agent results in a well-recognized syndrome of central nervous system and respiratory depression. Recently, a withdrawal syndrome has been described for GHB. We report a severe form of GBL withdrawal, characterized by delirium, psychosis, autonomic instability, and resistance to benzodiazepine therapy. METHODS: We performed a chart review of consecutive admissions for GBL withdrawal in a regional toxicology treatment center. RESULTS: During a 6-month period, 5 patients presented with severe withdrawal attributed to abrupt GBL discontinuation. Patients manifested tachycardia, hypertension, paranoid delusions, hallucinations, and rapid fluctuations in sensorium. Test results for ethanol and routine drugs of abuse were negative. Initial treatment with high doses of lorazepam proved ineffective. Pentobarbital was then administered, resulting in excellent control of behavioral, autonomic, and psychiatric symptoms and in rapid reduction or avoidance of benzodiazepines. Median hospital stay was 5 days. No patient had respiratory depression or required mechanical ventilation. Patients were discharged on tapering doses of benzodiazepines or pentobarbital and were free of psychotic symptoms at follow-up. CONCLUSION: GBL discontinuation can result in severe withdrawal, necessitating ICU admission. Pentobarbital may be more effective than benzodiazepines at controlling delirium in patients with abnormal vital signs, paranoid delusions, and hallucinations as a result of GBL withdrawal.

GHB-Dangerous, Addictive and Uncontrollable "Party Drug", [Article in Swedish] **Persson SA, Eriksson A, Hallgren N, Eklund A, Berkowicz A, Druid H.,** Lakartidningen 2001 Sep 19; 98(38):4026-31, 4033-5.
This report reviews the pharmacology, toxicity and abuse pattern of gamma-hydroxybutyrate (GHB). The legislative changes pertaining to this substance are also addressed. Examples of abuse, driving under the influence and fatal intoxication are given. It is concluded that GHB is widely abused, particularly among the younger generation, and that further cases of severe intoxication are likely to occur as long as the substance is easily available from countless sources, including via the Internet. Despite the classification of GHB as a narcotic in Sweden and several other countries, continued problems are expected since the precursors gamma-butyrolactone (GBL) and 1,4-butanediol (BD) are widely--and legally--available.

A contemporaneous finding of fenproporex in a polydrug suicide., Bell RR, Crookham SB, Dunn WA, Grates KM, Reiber TM., J Anal Toxicol 2001 Oct;25(7):652-6.
Fenproporex is a sympathomimetic agent with a pharmacological profile similar to that of amphetamine. It is available in many countries throughout the world, but it is currently not available in the United States. Because of its stimulant effects, it has a great potential for abuse. To the best of our knowledge, there have been no literature reports of blood or serum concentrations found in therapeutic, toxic, or fatal cases. We report a case where fenproporex was a finding in the death of a young adult. Blood, urine, and gastric contents were analyzed. The following drug concentrations were found: 0.90 mg/L (inferior vena cava blood), 1.2 mg/L (urine), and 120 mg total (gastric) for fenproporex and 0.084 mg/L (inferior vena cava blood), 0.94 mg/L (urine), and 0.14 mg total (gastric) for amphetamine. In addition to the fenproporex, other medications detected and their blood concentrations found in this case were H diazepam (0.54 mg/L), nordiazepam (0.46 mg/L), diphenhydramine (0.12 mg/L), and gamma hydroxybutyric acid (GHB) (1100 mg/L).

Gamma-hydroxybutyric acid: patterns of use, effects and withdrawal., Miotto K, Darakjian J, Basch J, Murray S, Zogg J, Rawson R., Am J Addict 2001 Summer;10(3):232-41.
Gamma-hydroxybutyric acid (GHB) is gaining popularity as a drug of abuse. Reports of toxicity and lethality associated with GHB use have increased. This survey study was designed to identify patterns of GHB use, its effects, and withdrawal syndrome. A survey inquiring about the effects of GHB was administered to 42 users. The results showed that GHB was used to increased feelings of euphoria, relaxation, and sexuality. Adverse effects occurred more frequently in daily users and polydrug users than in occasional GHB users. Loss of consciousness was reported by 66%, overdose by 28%, and amnesia by 13% of participants during GHB use and by 45% after GHB use. Three daily users developed a withdrawal syndrome that presented with anxiety, agitation, tremor, and delirium. Participants described GHB intoxication as having similarities to sedative-hypnotic or alcohol intoxication. Regular use has been shown to produce tolerance and dependence. Participants dependent on GHB reported using multiple daily doses around the clock. High frequency users appeared at the greatest risk for developing withdrawal delirium and psychosis after abrupt discontinuation of GHB use.

GHB. Club drug or confusing artifact?, Karch SB, Stephens BG, Nazareno GV., Am J Forensic Med Pathol 2001 Sep;22(3):266-9.
GHB can be produced either as a pre- or postmortem artifact. The authors describe two cases in which GHB was detected and discuss the problem of determining the role of GHB in each case. In both cases, NaF-preserved blood and urine were analyzed using gas chromatography. The first decedent, a known methamphetamine abuser, had GHB concentrations similar to those observed with subanesthetic doses (femoral blood, 159 microg/ml; urine, 1100 microg/ml). Myocardial fibrosis, in the pattern associated with stimulant abuse, was also evident. The second decedent had a normal heart but higher concentrations of GHB (femoral blood, 1.4 mg/ml; right heart, 1.1 mg/ml; urine, 6.0 mg/ml). Blood cocaine and MDMA levels were 420 and 730 ng/ml, respectively. Both decedents had been drinking and were in a postabsorptive state, with blood to vitreous ratios of less than 0.90. If NaF is not used as a preservative, GHB is produced as an artifact. Therefore, the mere demonstration of GHB does not prove causality or even necessarily that GHB was ingested. Blood and urine GHB concentrations in case 1 can be produced by a therapeutic dose of 100 mg, and myocardial fibrosis may have had more to do with the cause of death than GHB. The history in case 2 is consistent with the substantial GHB ingestion, but other drugs, including ethanol, were also detected. Ethanol interferes with GHB metabolism, preventing GHB breakdown, raising blood concentrations, and making respiratory arrest more likely. Combined investigational, autopsy, and toxicology data suggest that GHB was the cause of death in case 2 but not case 1. Given the recent discovery that postmortem GHB production occurs even in stored antemortem blood samples (provided they were preserved with citrate) and the earlier observations that de novo GHB production in urine does not occur, it is unwise to draw any inferences about causality unless (1) blood and urine are both analyzed and found to be elevated; (2) blood is collected in NaF-containing tubes; and (3) a detailed case history is obtained.

Schneir AB, et al., "A Case of Withdrawal from the GHB Precursors Gamma-butyrolactone and 1,4-butanediol", J.Emerg.Med., July 2001; 21(1):31-33.
A case of withdrawal from the gamma hydroxybutyric acid (GHB) precursors gamma butyrolactone and 1,4-butanediol are described. Symptoms included visual hallucinations, tachycardia, tremor, nystagmus, and diaphoresis. Administration of benzodiazepines and phenobarbital successfully treated the withdrawal symptoms. As predicted from the metabolism of gamma butyrolactone and 1,4-butanediol to GHB, the symptoms were nearly identical to those reported from GHB withdrawal. Because GHB is now illegal in the U.S., individuals have begun abusing the legal and easier to acquire GHB precursors. More frequent cases of both abuse and withdrawal from these GHB precursors can be expected.

GHB and Driving Impairment., Couper FJ, Logan BK., J Forensic Sci 2001 Jul;46(4):919-23.

Gamma hydroxybutyrate (GHB) was identified in the blood of 13 subjects arrested for impaired driving. GHB concentrations ranged from 26 to 155 mg/L (mean 87 mg/L, median 95 mg/L). In eight cases, GHB was the only drug detected, and signs of impairment were consistent with those of a CNS depressant, including erratic driving (weaving, swerving, ignoring road signs), confusion, incoherent speech, unresponsiveness, lack of balance,

unsteady coordination, poor performances on field sobriety tests, and varying states of wakefulness. Given the ability of GHB to induce sleep and unconsciousness, it is evident from these cases that recreational use of the drug has the potential to impair a person's driving ability.

Liquid ecstasy poisoning: study of 22 cases., Espinosa G, Miro O, Nogue S, To-Figuera J, Sanchez M, Coll-Vinent B., Med Clin (Barc) 2001 Jun 16;117(2):56-8. [Article in Spanish]
To describe characteristics of acute poisoning with liquid ecstasy (gammahydroxybutyrate, GHB). Epidemiological and clinical data of patients with acute GHB poisoning seen at emergency department (ED) along one year were collected. RESULTS: 22 patients were included. Typical profile corresponds to a young male, who consults on weekend, at night, complaining of a marked decreased level of consciousness. Patients refer coingestion of other drugs and typically regain consciousness spontaneously in a short time. CONCLUSION: The frequency of GHB poisoning has increased notably in our environment. GHB poisoning must be considered on the differential diagnostic of coma of unknown origin in young patients attended in ED.

"GHB: A New and Novel Drug of Abuse", Nicholson KL and Balster RL, , Drug Alcohol Depend., June 2001, 63(1): 1-22.
There has been increasing attention in the United States to problems of abuse of GHB, with some evidence for problems in other parts of the world as well. In vitro and animal research show that, while GHB shares some properties with abused central nervous system depressant drugs, it has unique aspects of its pharmacology as well, including actions at a specific neural receptor which probably mediates many of its effects. Abuse potential assessment of GHB using standard animal models has not yielded a picture of a highly abusable substance, but little human testing has yet been done. Very little systematic data exists on tolerance and dependence with GHB, but both have been seen in human users. Quantitative data on the prevalence of GHB abuse is incomplete, but various qualitative measures indicate that a mini-epidemic of abuse began in the late 1980s and continues to the present. GHB is often included with the group of "club drugs," and can be used as an intoxicant. It also has been used as a growth promoter and sleep aid and has been implicated in cases of 'date-rape', usually in combination with alcohol. Undoubtedly the easy availability of GHB and some of its precursors has contributed to its popularity. Recent changes in the control status of GHB in the US may reduce its availability with as yet unknown consequences for the scope of the public health problem. Drug abuse experts need to familiarize themselves with GHB as possibly representing a new type of drub abuse problem with some unique properties.

Blood, brain, and hair GHB concentrations following fatal ingestion., Kalasinsky KS, Dixon MM, Schmunk GA, Kish SJ., J Forensic Sci 2001 May;46(3):728-30.
Despite the increasing incidence of illicit use of gamma-hydroxybutyrate (GHB), little information is available documenting levels of the drug in GHB fatalities. We measured GHB levels in postmortem blood, brain and hair specimens from a suspected overdose case by gas chromatography/mass spectrometry (GC/MS) following solid phase extraction (SPE) and derivatization with bis(trimethyl-silyl) trifluoroacetamide (BSTFA). Examination found 330 microg/mL GHB in femoral blood and 221 ng/mg GHB in frontal cortex brain tissue, values higher than those typically reported in the literature. The hair shaft was negative for GHB whereas the plucked root bulbs with outer root sheath attached (2,221 ng/mg) and root bulbs after washing and removal of the outer root sheath (47 ng/mg) contained the drug. Our results are consistent with an acute single dose of GHB and, as the toxicology screen was negative for other drugs of abuse, emphasize the significant danger of this drug.

Gamma hydroxybutyrate (GHB) and gamma butyrolactone (GBL) withdrawal: five case studies., McDaniel CH, Miotto KA., J Psychoactive Drugs 2001 Apr-Jun;33(2):143-9.
There is little medical information available about gamma-hydroxybutyrate (GHB) or gamma-butyrolactone (GBL) dependence or withdrawal. In this study the authors treated and reviewed multiple cases of GHB and GBL withdrawal in high-dose users. Five patients during nine hospitalizations were treated for GHB or GBL withdrawal. The authors describe a spectrum of GHB or GBL withdrawal from mild to severe and discuss medications used for treatment. They conclude that patients with GHB or GBL withdrawal may present with agitated psychosis, delirium, and autonomic instability. In this sample, relapse to GHB or GBL use occurred soon after treatment of withdrawal.

GHB: An Important Pharmacologic and Clinical Update., Okun MS, Boothby LA, Bartfield RB, Doering PI., J Pharm Pharm Sci 2001 May-Aug;4(2):167-75.
Gamma-hydroxybutyrate (GHB) intoxication is a significant cause of morbidity and mortality in patients taking the drug for recreational purposes. Due to the recent increase in emergency room visits, hospital admissions, and deaths, it has become necessary to re-examine the pharmacology, pharmacokinetics, pharmacodynamics, clinical manifestations, and potential adverse effects associated with GHB use. We present an important pharmacologic and clinical update on GHB.

"The Urinary Excretion of Gamma-hydroxybutyric Acid in Man", Kavanaugh PV et al., ,J.Pharm. Pharmacol., March 2001, 53(3): 399-402.
GHB has been widely associated with drug-facilitated sexual assault. However, its excretion profile in man has not been well characterized. To assess the detectability of GHB for forensic cases and to correlate urinary levels with dose, we have examined the excretion profiles of 1- and 2-g doses of GHB (sodium salt) in a healthy male volunteer. The urinary levels were measured by a novel, simple and highly reproducible method. The drug was found to be excreted in small amounts in the free form (0.86 and 1.16% for 1- and 2- g doses, respectively) rapidly in urine (1 or = 10 h). The urinary levels were found to be in the low mg/L range (up to 29.1 mg/L). The work presented demonstrates that it is of the utmost importance to collect the samples as soon as possible following the alleged assault.

"Gamma-hydroxybutyrate Withdrawal Syndrome", Dyer JE et al., , Ann.Emerg.Med., February 2001, 37(2): 147 –153.
GHB withdrawal syndrome is increasingly encountered in emergency departments among patients presenting for health care after discontinued frequent GHB use. This report describes the characteristics, course, and symptoms of this syndrome. A retrospective review of poison center records identified 7 consecutive cases in which patients reporting excessive GHB use were admitted for symptoms consistent with a sedative withdrawal syndrome. One additional case identified by a medical examiner was brought to our attention. These medical records were reviewed extracting demographic information, reason for presentation and use, concurrent drug use, toxicology screenings, and the onset and duration of clinical signs and symptoms. Eight patients had a prolonged withdrawal course after discontinuing chronic use of GHB. All patients in this series were psychotic and severely agitated, requiring physical restraint and sedation. Cardiovascular effects included mild tachycardia and hypertension. Neurologic effects of prolonged delirium with auditory and visual hallucinations became episodic as the syndrome waned. Diaphoresis, nausea, and vomiting occurred less frequently. The onset of withdrawal symptoms in these patients was rapid (1 to 6 hours after the last dose) and symptoms were prolonged (5 to 15 days). One death occurred on hospital day 13 as withdrawal symptoms were resolving. In our patients, severe GHB dependence followed frequent ingestion every 1 to 3 hours around the clock. The withdrawal syndrome was accompanied initially by symptoms of anxiety, insomnia and tremor that developed soon after GHB discontinuation. These initial symptoms may progress to severe delirium with autonomic instability.

"Gamma-hydroxybutyrate (GHB): A Newer Drug of Abuse,", O'Connell T et al., Am.Fam.Physician, December 2000, 62(11): 2478-2483.
GHB is an illicitly marketed substance that has recently gained popularity among body builders and party attendees as a drug of abuse. GHB is a depressant that acts on the central nervous system. It is purported as a strength enhancer, euphoriant and aphrodisiac and is one of several agents reported as being used as a "date rape" drug. Because of its central nervous system depressant effects, GHB can be lethal when combined with alcohol or other depressants. Currently, there is no accepted medical use for GHB, and the U.S. Food and Drug Administration has prohibited its manufacture and sale. Clinicians should be familiar with the typical clinical presentation of GHB and its adverse effects. In addition patients should be warned of it potential toxicity and be cautioned to avoid the use of GHB.

"Gamma-hydroxybutyrate, gamma-butyrolactone, and 1,4-butanediol: A Case Report and Review of the Literature," Shannon M and Quang LS., Pediatr.Emerg.Care, December 20000, 16(6):435-440.

GHB, GBL, and 1,4-BD are prevalent drugs of abuse in the United Sates. Unfortunately, attempts to regulate GHB have been circumvented by clandestine trafficking through the Internet and marketing of "natural" chemical precursors. Despite repeated FDA warnings to the public about their dangers as well as recent Federal scheduling of GHB and GBL, they remain accessible as "club drugs" on Internet web sites, as natural dietary supplements in health food stores, and as illicit products manufactured at home or in clandestine laboratories. EDs and Poison control centers nationwide will undoubtedly continue to manage GHB, GBK, and 1,4-BD toxicity.

"Verve and Jolt: Deadly New Internet Drugs," Winickoff JP et al., Pediatrics, October 2000, 106(4): 829-830.
As regulatory agencies have increased restrictions on the sale and marketing of gamma-hydroxybutyrate (GHB), they have been frustrated by the appearance of precursor molecules such as gamma-butyrolactone (GBL) that have become widely available over the Internet. These dangerous precursors are vigorously marketed to adolescents and young adults as dietary supplements that increase muscle mass and enhance sexual performance with seductive names such as Verve and Jolt, both easily recognizable teen icons. We present the case of an adolescent who ingested both of these GBL products 2 weeks apart, resulting in life-threatening respiratory depression and emergent intubation on both occasions. The GBL toxidrome, necessary acute interventions, and public health implications are reviewed. We urge all health care providers to report similar cases immediately to the FDA MEDWatch system.

"Gamma-hydroxybutyric Acid (GHB): An Increasing Trend in Drug Abuse," Boyce SH et.al., Eur.J.Emerg.Med., September 2000, 7(3), 177-181.
The use of recreational drugs in society is becoming a widespread problem increasing the workload of all the emergency services. GHB is one of these, a drug used primarily for its euphoric effect. Toxic effects of ingestion include brandycardia, slow respiration or apnea, coma and death. We present seven cases, all of which had consumed GHB either alone or in conjunction with other drugs or alcohol. The presentation, clinical features and management of these cases are described. All health care personnel involved in the emergency setting need to know of its existence, toxic effects and initial management with particular reference to airway control and possible assisted ventilation.

Placement of Gamma-butyrolactone (GBL) in List I of the Controlled Substances Act (21 U.S.C.802 (34)). Drug Enforcement Administration, Justice. Final Rule., Federal Register, 24 April 2000, 65(79): 21645-21647.
Public Law 106-172, signed into law on February 18, 2000, and known as the "Hillory J. Farias and Samantha Reid Date-Rape Drug Prohibition Act of 1999," amends section 102(34) of the Controlled Substances Act (CSA) as amended by designating GBL, the precursor to GHB, as a List I chemical. Reflecting this change in stature, the DEA is amending its regulation to reflect the status of GBL as a List I chemical subject to the requirements of the CSA and its regulations. Establishment of a threshold for GBL will be the subject of a separate rulemaking. Therefore, unless and until a threshold is established, any distribution of GBL must comply with the CSA regulatory requirements pertaining to List I chemicals as described in the body of this document.

"Drug-facilitated Sexual Assault (date-rape)," Schwartz RH et.al. , Soth.Med.J., June 2000, 93(6): 558-561.
In the past few years, drug-facilitated sexual assaults have received widespread media coverage. In addition to alcohol, the most frequently used date-rape drug, flunitrazepam (Rohypnol), a fast acting benzodiazepine, and GHB and its congeners are among the most popular drugs used for this purpose. The latter drug is easily procured at some gymnasiums, popular bars, discos, and rave clubs, as well as over the Internet. Perpetrators choose these drugs because they act rapidly, produce disinhibition and relaxation of voluntary muscles, and cause the victim to have lasting anterograde amnesia for events that occur under the influence of the drug. Alcoholic beverages potentiate the drug effects. We review several date-rape drugs, provide information on laboratory testing for them, and offer guidelines for preventing drug facilitated sexual assault.

"Involvement of Drugs in Sexual Assault," Slaughter L.,, J.Reprod.Med., May 2000, 45(5): 425-430.
To obtain information about the relationship of alcohol and drug usage in victims of sexual assault, including the newly identified "date-rape" drugs GHB and Rohypnol (flunitrazepam). Analysis of urine samples with gas chromatography combined with mass spectrometry can identify alcohol and numerous other drugs with a high

degree of specificity. This service was offered to rape treatment centers throughout the U.S. in May 1996; urine samples obtained from sexual assault victims suspected of drug use by history or physical examination were sent for testing at the discretion of the examiner. As of March 1999, a total of 2,003 specimens were analyzed. Nearly two-thirds of the samples contained alcohol and/or drugs; the predominant substances found were alcohol, present in 63%, and marijuana, present in 30%. A substantial subset of the specimens was found to contain other illicit substances, frequently in combination. GHB and Rohypnol were found in less than 3% of the positive samples. Additionally, over the two-year study period, the use of these two drugs appeared to be declining. These findings support prior data indicating that alcohol, marijuana and/or other drugs are important risk factors in sexual assault. Continued monitoring of drug use by victims of sex crimes is important, and programs that serve victims should modify protocols to reflect this.

"A New Drug Reaches Switzerland: Coma After Intake of GHB," Iten PX et.al., Schweiz.Med.Wochenschr., March 2000, 130(10): 356-361. (Article In German)
The new recreational drug GHB reached Switzerland in 1998. We describe two cases from the city of Zurich. In both of them the subjects were profoundly unconscious and needed hospitalization after intake of a colorless liquid. Both patients recovered after a few hours, rapidly and without after-effects. GHB is abused mainly for its euphorigenic and sedative properties by young people in discos, at raves, or on the drug scene. It is also taken as an alleged anabolic agent among body builders. Criminals use it to narcotize potential victims. We summarize its effects, adverse effects, diagnosis, treatment, toxicology, pharmacology, and medical applications.

"Severe GHB Withdrawal: A Case Report and Literature Review," Craig K et.al., J.Emerg.Med., January 2000, 18(1): 65-70.
We report a case of GHB withdrawal resulting in severe agitation, mental status changes, elevated blood pressure and tachycardia hours after stopping chronic use of GHB. The patient admitted to substantial GHB abuse on a daily basis for 2.5 years. Previous attempts at cessation reportedly resulted in diaphoresis, tremors, and agitation. The patient's symptoms, negative polypharmacy history, and negative urine and blood toxicological analysis for alcohol, benzodiazepines, sedative-hypnotics, or other substances suggested the diagnosis of GHB withdrawal. Later analysis of a patient drug sample confirmed the presence of GHB. The patient required 507 mg of lorazepam and 120 mg of diazepam over 90 hr to control agitation. This is one of the few reported cases of GHB withdrawal and one of the most severe. Given the increasing use of GHB, more cases of severe GHB withdrawal should be anticipated.

"Poisoning with GHB: Cases Reported in Connection with "Cultural Festivals" Hunderup MC and Jorgensen AJ,, in August 1999 in Kolding," Ugeskr.Laeger., December 1999, 161(50): 6939-6940. (Article In Danish)
Eight cases of poisoning with the relatively newly introduced synthetic drug GHB are reported. The abuse of GHB was in most cases mixed with alcohol intake but not any opiates. The condition of some of the victims was serious with bradycardia and depressed respiration. The antidote (Naloxone) appeared to have a beneficial effect on the combined intoxication of GHB and alcohol.

, "GHB, A New Central Nervous System Stimulant," Strange DG and Jensen D, Ugeskr.Laeger., December 1999, 161(50): 6934-6936. (Article In Danish)
In the last months we have seen an increasing number of younger patients admitted to the emergency room in a deep coma, mostly without cardiopulmonary symptoms. After a few hours they suddenly woke up without any after-effects. Subsequently the patients related that they had taken an unknown drug for recreational purposes and afterwards fell asleep. The patients did not remember anything else about the episode. We believe they had taken GHB. This drug has not previously been described in Danish scientific reports.

"GHB—An Endogenous Substance and a New Central Nervous System Stimulant. Clinical Aspects of Acute Poisoning," Engelsen J and Christensen HR, Ugeskr.Laeger., December 1999, 161(50): 6903-6907. (Article In Danish)
During the last six months, the Poison Control Center at Bispebjerg Hospital, Copenhagen, Denmark, has observed an increasing number of patients intoxicated with GHB, a drug of abuse. The patients are often admitted to the emergency ward shortly after having taken the drug, unconscious or comatose. If younger patients

present with these symptoms, intoxication with GHB should be seriously considered. The effects are seen within 15 to 30 minutes after oral ingestion of the drug. Spontaneous recovery usually occurs within three to five hours. The most common effects are mild euphoria, sedation, vomiting, somnolence, bradycardia, aggressive behavior, apnea, respiratory depression, and coma. Normally the patient breathes adequately, but insufficient respiration may occur and deaths have been described. The drug is often consumed together with alcohol and other drugs of abuse, which strengthens the effect of GHB. Treatment is symptomatic. A review of the literature with special emphasis on clinical effects included toxicology and treatment given.

"Life-threatening Interactions Between HIV-1 Protease Inhibitors and the Illicit Drugs MDMA and Gamma-hydroxybutyrate" Harrington RD et.a.l., Arch.Intern.Med., October 1999, 159(18): 2221-2224**.**
HIV-1 protease inhibitors have dramatically reduced the morbidity and mortality due to HIV-1 infections. However, most of these antiretrovirals are also potent inhibitors (and occasionally inducers) of hepatic and intestinal cytochrome P450 systems and, therefore, have the potential to alter the elimination of any substance that utilizes these metabolic pathways. We describe a patient infected with HIV-1 who was treated with ritonavir and saquinavir and then experienced a prolonged effect from a small dose of MDMA and a nearly fatal reaction from a small dose of GHB. We also discuss the potential for HIV-1 protease inhibitors to alter the metabolism of other abusable prescribed and illicit substances.

"New Synthesis Empathogenic Agents", Velea D et.al., Encephale, September 1999, 25(5): 508-514 (Article In French)
The use of synthesis drugs is the object of numerous written articles and TV programs in the last decade. These synthesis drugs or designer drugs, are well known for their ability to enhance, reinforce or appease social difficulties and relationships. In the research for empathetic and entactogenic relations one discovers an obvious lack of communication and warmth in personal or professional relationship. An image of chemical "well-being" has become a frequent stereotype of a society with an atrophying of performance and values while supposedly dedicating itself to individual performance. The youths are the first victims of these new drugs, the economical and social environment are the main reinforcing factors of this behavior. The main characteristic of these drugs, is the non-recognition of their danger, some users go so far as to describe this category of substances as "drugs which are not drugs". As a characteristic, the use of these synthesis drugs is almost recreational, during the week-end and holiday. The drug addiction is different than that of opiates or cocaine. One can observe some cases of real dependence—corresponding to the DSW IV criterion—when the personality of the users is the main characteristic (narcissic failure, immature personality, family and school problems). Many adverse effects—hypertension, kidney failure, psychoses—were declared. The mass-media has presented many articles concerning MDMA. This is the most used drug during the rave parties. Its adverse effects are well known and proven. The authors would like to present other more recent synthesis drugs, also known as "analogues". These drugs, a kind of mixture between amphetamine-like (MDMA, MBDB, MDA) and misused medicines (ketamine, GHB, atropine) represent a real danger. GHB, 2CB, HMB, are some of these recent substances. The possibility to procure them on the Web, or to produce them by oneself add to their danger because of the lack of controls on toxicity and quality. The original danger signs were revealed by the FDA and currently a major preoccupation within French specialized services. The major problem for the practitioner is to inform the users, in order to prevent addiction and analyze the solutions.

"Drugs Used in Acquaintance Rape," Smith KM., J.Am.Pharm.Assoc., July 1999, 39(4): 519-525.
To describe GHB, flunitrazepam, and ketamine and their purported uses to facilitate acquaintance rape. Patient presentation characteristics, treatment regimens, processes to detect the presence of the medications by toxicology screening, and methods to avoid exposure are discussed. Reports of the use of GHB, flunitrazepam, and ketamine in acquaintance rape appear in the medical literature and lay press. Many health care professionals may not be familiar with these medications, and information about caring for patients under their influence is limited. Victims lose their ability to ward off attackers, develop amnesia, and are unreliable witnesses. Because symptoms caused by these agents mimic those of alcohol, not all victims are screened for their presence. Legislative efforts to further limit the use of or access to GHB, flunitrazepam, and ketamine have been initiated at the state and Federal levels (Passed in Public Law 106-172 of Feb 18, 2000). Pharmacists should know the symptoms of exposure to these three agents; they should understand treatment regimens, methods to detect the presence of these and other drugs that may have been used in a sexual assault, and techniques individuals can use to avoid

becoming victims of drug-assisted acquaintance rape. Because of their extensive drug knowledge and frequent access to patients, pharmacists are uniquely positioned to educate patients and other health professionals about the dangers of acquaintance rape drugs and methods to reduce their risk of becoming victims.

"Prevalence of Drugs Used in Cases of Alleged Sexual Assault," Elsohly MA and Salmone SJ., J.Anal.Toxicol, May 1999, 23(3): 141-146.
In recent years, there has been an increase in the number of reports in the U.S. of the use of drugs, often in conjunction with alcohol, to commit sexual assault. A study was undertaken to assess the prevalence of drug use in sexual assault cases in which substances are suspected of being involved. Law enforcement agencies, emergency room, and rape crises centers across the U.S. were offered the opportunity to submit urine samples collected from victims of alleged sexual assault, where drug use was suspected, for analysis of alcohol and drugs which may be associated with sexual assault. Each sample was tested by immunoassay for amphetamines, barbiturates, benzodiazepines, cocaine metabolite, cannabinoids, methaqualone, opiates, phencyclidine and propoxyphene. The positive screen results were confirmed by gas chromotography mass spectrometry (GC-MS). In addition, each sample was tested for flunitrazepam metabolites and GHB by GC-MS and for ethanol by GC-flame ionization detection. Over a 26-month period, 1179 samples were collected and analyzed from 49 states, Puerto Rico, and the District of Columbia. Four-hundred sixty eight of the samples were found negative for all the substance tested; 451 were positive for ethanol, 218 for cannabinoids, 97 for benzoylecgonine, 97 for benzodiazepines, 51 for amphetamines, 48 for GHB, 25 for opiates, 17 for propoxyphene, and 12 for barbiturates. There were no samples identified as positive for PCP or methaqualone. In addition, 35% of the drug-positive samples contained multiple drugs. This study indicates that, with respect to alleged sexual assault cases, the prevalence of ethanol is very high, followed by cannabinoids, cocaine, benzodiazepines, amphetamines, and GHB. Although only a couple of substances have been implicated with sexual assault, this study has shown that almost 20 different substances have been associated with this crime. This study also raises the concern of illicit and licit drug use in sexual assault cases and suggests the need to test for GHB, which is not generally tested for in a normal toxicology screen.

"Toxic Ingestion of GHB", Viera AJ and Yates SW., South.Med.J., April 1999, 92(10): 1037.
GHB has become a popular new drug of abuse. Its effects include euphoria and disinhibition. Recently, several cases have been reported in the literature of life-threatening or lethal ingestion. We report the case of a 17-year old male who became unresponsive after taking GHB. GHB is used outside the U.S. to treat narcolepsy. In the past, it was touted as a muscle-bulking aid and was taken by body-builders. It has also been implicated as a drug involved in "date-rapes." Patients who ingest excessive GHB have a markedly altered level of consciousness, as did the patient in this illustrative case. Neostigmine and physostigmine show promise as potential reversal agents. GHB overdose should be considered in any patient with altered mental status and a history of recreational drug abuse.

"Adverse Events Associated with Ingestion of Gamma-butyrolactone (GBL) --Minnesota, New Mexico, and Texas, 1998-1999. MMWR Morb.Mortal.Wkly.Rep., 26 February 1999, 48(7): 137-140.
Products containing GBL are marketed for many claimed purposes including: to induce sleep, release growth hormone, enhance sexual activity and athletic performance, relieve depression, and prolong life. GBL is converted by the body into GBH, a drug banned outside of clinical trials approved by the FDA. Recognized manifestations of GHB toxicity include bradycardia, hypothermia, central nervous system depression, and uncontrolled movements. This report describes seven cases of GBL toxicity involving the product "Revivarant," which is labeled as containing 1.82 g of GBL per fluid ounce, reported from two hospital emergency departments in Minnesota during October-December 1998 and summarizes an additional 34 cases of GBL toxicity reported to poison centers in New Mexico and Texas during October 1998-January 1999.

"Clinical Course of GHB Overdose," Chin RL et.al., Ann.Emerg.Med., June 1998, 31(6): 716-722.
To describe the clinical characteristics and course of GHB overdose. We assembled a retrospective series of all cases of GHB ingestion seen in an urban public-hospital emergency department and entered in a computerized database January 1993 through December 1996. From these cases we extracted demographic information,

concurrent drug use, vital signs, Glasgow Coma Scale (GCS) score, laboratory values, and clinical course. Sixty-one (69%) of the 88 patients were male. The mean age was 28 years. Thirty-four cases (39%) involved coingestion of ethanol and 25 (28%) involved coingestion of another drug, most commonly amphetamines. Twenty-five cases (28%) had a GCS score of 3, and 28 (33%) had scores ranging from 4 through 8. The mean time to regained consciousness from initial presentation among non-intubated patients with an initial GCS of 13 or less was 146 minutes Range, 16-389). Twenty-two patients (36%) had asymptomatic bradycardia; in 29 of these cases, the initial GCS score was 8 or less. Ten patients (11%) presented with hypotension (systolic blood pressure less than or equal to 90 mm Hg); 6 of these patients also demonstrated concurrent bradycardia. Arterial blood gases were measured in 30 patients; 21 had a PCO2 of 45 or greater, with pH ranging from 7.24 to 7.34, consistent with mild acute respiratory acidosis. Twenty-six patients (30%) had an episode of emesis; in 22 of these cases, the initial GCS was 8 or less. In our study population, patients who overdosed on GHB presented with a markedly decreased level of consciousness. Coingestion of ethanol or other drugs is common, as are bradycardia, hypthermia, respiratory acidosis, and emesis. Hypotension occurs occasionally. Patients typically regain consciousness spontaneously with 5 hours of the ingestion.

"Gamma-hydroxybutyrate (GHB): A New Drug of Misuse," Williams H. et.al., Ir.Med.J., March 1998, 91(2): 56-57.
Accident and Emergency Departments offer a unique opportunity for identifying and monitoring new drugs of misuse. This series of six case reports describe the potentially serious medical complications associated with the use of GHB, a new drug of misuse on the UK scene. Profound unconsciousness occurred in all cases and despite full (and often rapid) recovery all patients required medical intervention. Adverse effects occurred both when GHB was used alone or in combination with other illicit drugs and alcohol.

"Pediatric Gamma-hydroxybutyrate Intoxication," Suner S. et.al., Acad.Emerg.Med., November 1997, 4(11): 1041-1045.
Reported are 2 uncommon cases of childhood GHB toxicity and the surreptitious manner in which GHB was made. Two children unintentionally ingested a soft drink containing GHB and were found comatose. Both had been well 1 hour earlier. The parent had made GHB by combining gamma butyrolactone with caustic soda (sodium hydroxide). Symptoms were early in onset and resolved in 24 hours. The ECG changes in one case are unique to GHB toxicity and are unexplained. GHB-toxic children appear similar to adults who have this poisoning. Supportive management remains the mainstay of therapy. Health care providers should be aware of GHB's clandestine production and its increasing presence on the streets and in the home. This agent is not detected with common drug screens.

The following three articles are included for awareness. GHB is used in parts of Europe since 1991, in the management of alcohol withdrawal syndrome. It was reported to be as effective and perhaps better than the use of benzodiazepine for this purpose. However, withdrawal symptoms associated with the use of GHB are now being reported. The one article below and two articles referenced above report GHB withdrawal symptoms. The three articles below are to provide background on the use of GHB as a clinical management tool in alcohol withdrawal syndrome in European medical practice.

Addolorato G. et.al., "A Case of Gamma-hydroxybutyric Acid Withdrawal Syndrome During Alcohol Addiction Treatment: Utility of Diazepam Administration," Clin.Neuropharmacol, January 1999, 22(1): 60-62.
GHB is an emerging drug for alcoholism therapy. We present a case of GHB withdrawal syndrome secondary to GHB addition during alcoholism treatment. A complete disappearance of drug withdrawal syndrome was achieved with oral diazepam and the symptoms resolved without sequelae. GHB has been used for alcoholism therapy for only a few years now, but the trend is increasing, and other cases similar to this one are foreseeable. This risk could be higher in some countries in which GHB use is increasing not for alcoholism therapy, but for its

euphoric and anabolic effects. The present experience indicates that administration of benzodiazepines would seem to be sufficient to achieve total regression of the withdrawal syndrome in a short time, at least if recognized early.

Addolorato G. et.al., "Gamma-hydroxybutyric Acid (GHB) in the Treatment of Alcohol Withdrawal Syndrome: A Randomized Comparative Study Versus Benzodiazepine," Alcohol Clin.Exp.Res., October 1999, 23(10): 1596-1604.

Benzodiazepine has been shown to be one of the most effective class of drugs in the management of alcohol withdrawal syndrome (AWS). GHB has recently been introduced in the treatment of alcohol problems, including AWS. At present there are no comparative studies between benzodiazepines and GHB in AWS treatment. The aim of the present randomized, controlled, single-blind study was to evaluate the efficacy and safety of GHB compared with diazepam in the treatment of AWS. Sixty alcoholics affected by AWS were enrolled in the study. Diazepam (0.5-0.75 mg/kg body weight for 6 days, tapering the dose 25% daily until day 10) was administered orally to 30 patients (25 males, 5 females; mean age 44.3 +/- 10.9 years); GHB (50 mg/kg body weight for 10 days) was administered orally to 30 patients (26 males, 4 females; mean age 41.7 +/- 10.4 years). The Clinical Institute Withdrawal Assessment for Alcohol revised scale (CIWA-Ar) was used to evaluate the AWS physical symptoms. The State Anxiety Inventory test for current anxiety assessment and the Zung self-rating Depression Scale for current depression assessment were performed. RESULTS: Eight patients (26.6%) in the diazepam group and 4 patients (13.3%) in the GHB group dropped out. Both treatments were effective in reducing AWS. No significant difference was found between the groups in CIWA-Ar total score at baseline and at the different times of observation. Considering the CIWA-Ar subscore and Zung scale, a significant reduction of anxiety on day 4 ($p<0.02$), agitation on day 5 ($p<0.02$) and time of recovery of depression on day 5 ($p<0.02$) was observed in the GHB group with respect to the diazepam group. Drowsiness and vertigo developed after initial drug administration in the GHB (19.2%) and diazepam (36.4%) groups and quickly resolved in both groups. CONCLUSION: GHB is as effective in the management of AWS as benzodiazepine and it seems to be quicker in reducing anxiety, agitation, and depression. Both drugs are safe and well-tolerated in AWS management.

Beghe F and Carpanini MT., "Safety and Tolerability of Gamma-hydroxybutyric Acid in the Treatment of Alcohol-dependent Patients," Alcohol, April 2000, 20(3): 223-225.

GHB has been in clinical use in Italy since 1991 for treatment of alcohol dependence. Results of phase III and phase IV studies have shown that the drug is effective and well tolerated in the treatment of alcohol withdrawal syndrome and in reducing alcohol consumption and alcohol craving. Pharmacosurveillance indicates that abuse of GHB is a limited phenomenon in clinical settings when the drug is dispensed under strict medical surveillance and entrusted to a referring familiar member of the patient.